Editorial: palliative long-term abdominal drains in refractory ascites – a step in the right direction, but not the complete solution. Authors' reply

Article (Accepted Version)

Editorial: palliative long-term abdominal drains in refractory ascites – a step in the right direction, but not the complete solution. Authors' reply

Lucia Macken, Stephen Bremner, David Sheridan and Sumita Verma, on behalf of the REDUCe study team.

We thank Dr Hudson for his balanced and insightful editorial (1). We are in agreement that palliative care remains woefully inadequate in end-stage liver disease. Reasons are multiple and complex but include lack of evidence-based interventions. The REDUCe study (2) addressed feasibility to proceed to a definitive trial, our ultimate aim being to improve palliative management of refractory ascites in end-stage liver disease.

Primary prophylaxis for spontaneous bacterial peritonitis remains a contentious issue and is the subject of ongoing studies (ASEPTIC EurdaCT number 2019-000581-38). Guidance is to use antibiotic prophylaxis in advanced liver disease if ascitic fluid protein is $\leq$ 15 g/L (3-4). Recent studies however suggest that ascitic fluid protein may not predict spontaneous bacterial peritonitis (5-6). Nonetheless, there is consensus that severe liver disease is a risk factor for spontaneous bacterial peritonitis (7-8). Since refractory ascites reflects advanced liver disease with a median survival of six months (3, 9), in our feasibility study, we pragmatically offered all research participants prophylactic antibiotics for the study duration. Discussions with Hepatologists and Palliative Care specialists who had experience in using LTAD in end-stage liver disease supported this strategy. We do nonetheless acknowledge that antibiotic use is not without risks.

Having demonstrated feasibility, the next step would be a definitive study comparing LTAD versus large volume paracentesis in refractory ascites due to end-stage liver disease. Since infection remains a major deterrent to use of LTAD in cirrhosis, an appropriate primary outcome would be non-inferiority peritonitis incidence, with quality of life as one of the

secondary outcomes. We would again support use of prophylactic antibiotics in study participants, thus assessing incidence of spontaneous bacterial peritonitis after primary prophylaxis. The overarching goal, as endorsed by our service users, is to avoid repeated hospitalisation.

Dr Hudson makes a valid point that use of LTAD is only part of the solution in end-stage liver disease. We however hope that the feasibility and any potential future definitive trial will encourage wider discussions amongst hospital and community teams, thus increasing knowledge, skills and confidence in managing end-stage liver disease in the community. It could also raise the profile of this disenfranchised cohort, promoting equality in end of life care and initiating discussions about future research priorities.

The authors' declarations of personal and financial interests are unchanged from those in the original article (2).

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